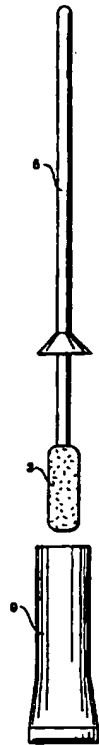


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(21) International Application Number: PCT/US96/02734 (22) International Filing Date: 29 February 1996 (29.02.96) (71) Applicant (for all designated States except US): ZILA PHARMACEUTICALS, INC. [US/US]; 5227 North 7th Street, Phoenix, AZ 85014-2800 (US). (72) Inventor; and (75) Inventor/Applicant (for US only): HINES, Joseph [US/US]; 4525 E. Pescar Drive, Paradise Valley, AZ 85253 (US). (74) Agents: DRUMMOND, William, H. et al.; Drummond & Duckworth, Suite 500, 4590 MacArthur Boulevard, Newport Beach, CA 92660 (US).		(81) Designated States: AU, CA, JP, KR, RU, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i>
(54) Title: METHOD AND PREPACKAGED SWAB STICK FOR EPITHELIAL CANCER SCREENING (57) Abstract <p>A prepackaged swab stick for performing routine screening procedures to detect possible epithelial cancer. The prepackaged swab stick including a packet (7) encasing an absorbent swab (3). The swab (3) is disposed at the extremity of a handle (5) and is saturated with a liquid testing reagent.</p> 		

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**METHOD AND PREPACKAGED SWABSTICK
FOR EPITHELIAL CANCER SCREENING**

BACKGROUND

5 This invention relates to improved methods for screening patients for
epithelial cancer.

In another respect, the invention relates to a prepackaged swabstick for use
in screening patients to detect possible epithelial cancer.

10 More particularly, the invention pertains to a prepackaged swabstick for
use in screening patients for epithelial cancer which can be used by para-
professional medical personnel without highly specialized training.

In yet another respect, the invention pertains to a prepackaged swabstick
for use in screening patients for epithelial cancer, which places liquid diagnostic
reagents at the immediate disposal of clinical personnel, without requiring time-
consuming or complicated mixing-storage-dispensing-measuring steps.

15 Various procedures are known for screening patients for epithelial cancer,
especially for detecting suspected cancerous and precancerous sites on the mucosa
such as the oral mucosa. Such procedures generally employ a dye which
preferentially stains RNA-rich tissues which have been recognized as characteristic

of cancerous and precancerous conditions. For example, U.S. Patent to *Mashberg* No. 4,321,251, discloses such a procedure. The procedure of *Mashberg* involves sequential washes, rinses and applications of water, dilute acidic acid and a solution of toluidine blue O dye, in the mouth to detect cancerous and
5 precancerous conditions of the oral mucosa. This wash-rinse-application-rinse-wash procedure is then repeated after 10-14 days when a suspect site is detected, to reduce the number of false positives. Each repetition of the procedure involves a pre-rinse with acetic acid, two pre-rinses with water, a rinse with toluidine blue O dye, a post-rinse with acetic acid and a post-rinse with water.

10 It would be highly advantageous to screen all patients for epithelial cancer during routine office visits such as visits to dental offices for teeth cleaning, etc. However, methods of screening for epithelial cancer such as the *Mashberg* procedure have not achieved routine use, because the mixing, measuring and dispensing the solutions required is messy and too time consuming to be done for
15 each patient by the dentist and such procedures require some training and experience beyond that normally possessed by para-professional assistants.

Further, the devices for delivering the liquid testing reagent to the suspected cancerous or precancerous sites are crude and cumbersome and generally not accepted by medical doctors and dentists. For example, present
20 cancer screening procedures require that the reagent, for example toluidine blue, be administered by rising the entire mouth with the reagent or by applying the reagent directly to the suspected cancerous or precancerous site by using a

saturated swab. Rinse applications require that the liquid reagent be poured from a larger container into a small cup to facilitate introducing the reagent into the mouth of a patient. Likewise, swab application requires that the absorbent swab be placed into a container containing the liquid reagent. The swab is then
5 removed from the container and inserted into a patient's mouth to apply the reagent to the suspect cancerous or precancerous site. Each of these procedures is susceptible to spillage from the reagent container, reagent-containing cup or swab. Even a slight amount of spilled dye reagent can be extremely undesirable due to the inherent staining properties of the dye.

10 Clinical swabs are utilized for many purposes such as cleaning wounds and applying anesthetics or disinfectants to body tissue. Prepackaged swabs are known. For example, the Clinipad Corporation manufactures a prepackaged swab sold under the mark Cliniswab. The Cliniswab kit includes a swab attached to the end of a plastic stick encased in a packet. The swab is of an absorbent material
15 such as cotton and is saturated with an antiseptic or cleansing liquid such as iodine or isopropyl alcohol.

It would therefore be desirable to provide an improved method for screening patients for epithelial cancer which is simplified and especially adapted to promote routine screening as the adjunct to normal visits by patients to medical
20 or dental offices for other reasons.

Accordingly, the principal object of the present invention is to provide such improved screening methods.

Yet another object of the invention is to provide apparatus which encourages such routine testing, by minimizing the time and complications which formally discouraged such routine testing by medical and dental professionals.

SUMMARY

The present invention provides an improved method and apparatus for performing routine screening procedures to detect possible epithelial cancer. The method is an improvement of prior art screening methods, which includes applying to suspected cancerous or precancerous sites a liquid testing reagent of preselected concentration. The improved method comprises applying the testing reagent with a prepackaged swab to permit dispensation of the reagent directly from its package with a for use in accordance with the screening procedure, without further mixing or measuring.

The apparatus of the present invention includes a swab saturated with the liquid testing reagent attached to the end of a handle. The swabstick is encased in a packet to facilitate handling of the testing reagent and minimize spillage prior to application to the suspected cancerous or precancerous sites.

In accordance with the apparatus and method of the present invention, the prepackaged swabstick eliminates the mixing and measuring steps generally required of administering clinicians to prepare and apply a diagnostic reagent to a suspected cancerous or precancerous site on the oral mucosa.

5 An advantage of the present invention is a simplified screening method which will promote routine epithelial cancer screening during normal visits by the patients to medical or dental offices.

 An additional advantage of the present invention is to eliminate the need for para-professional assistants by providing a simplified method of applying a testing
10 reagent to suspected cancerous or precancerous sites of epithelial cancer.

 Moreover, the present invention reduces or completely eliminates the damage to medical offices due to staining from the unexpected release or spillage of the liquid testing dye.

 Other features and advantages of the present invention will be appreciated
15 by those skilled in the art upon reading the detailed description which follows with reference to the attached drawing.

BRIEF DESCRIPTION OF THE DRAWINGS

These and other features, aspects and advantages of the present invention, will become better understood to those skilled in the art from the following description, appended claims and accompanying drawing where:

5 Figure 1 depicts a prepackaged swabstick which is employed in accordance with principles of the present invention; and

Figure 2 depicts a preferred embodiment of the swabstick in accordance with principles of the present invention.

DETAILED DESCRIPTION

10 While the present invention is susceptible of embodiment in various forms, there is shown in the drawing and will hereinafter be described, a presently preferred embodiment of the invention, with the understanding that the present disclosure is to be considered as an exemplification of the invention, and I do not intend to limit the invention to the specific embodiments illustrated.

15 Referring to Figure 1, the prepackaged swabstick 1 includes a swab 3, a handle 5 and detachable cover 7. The swab 3 is of an absorbent material such as cotton and is affixed to the end of handle 5. As will be understood by those in the art, the handle could be manufactured from any of several biologically nonreactive

materials such as plastic or treated wood, and can be produced in any number of configurations. For example, Figure 1 discloses handle 5 being configured as a cylinder with a concentric bore communicating with a container 4 for receipt and storage of the liquid testing reagent. The swab 3 is saturated with a liquid testing reagent (not shown) such as the dye toluidine blue O, for applying to suspected to cancerous or precancerous sites on the oral mucosa. Encasing the swab 3 and handle 5 is a cover 7 detachable from the container 4 to prevent the release or spillage of the liquid testing reagent prior to application to the suspected cancerous or precancerous sites.

10 In another embodiment of the prepackaged swabstick, depicted in Figure 2, the liquid reagent (not shown) is carried in a cylindrical container 9. In this configuration, the handle 5 is flexed to break away from the upper end of container 9 to allow withdrawal of the swab 3, soaked with the liquid reagent.

In addition to the apparatus of a prepackaged swabstick, the present invention provides for improved methods for screening for epithelial cancer. A prepackaged swabstick of the present invention is provided to the administering clinician. After removing the swabstick from its package, the swab 3, being saturated with a liquid testing reagent, is applied to suspected cancerous or precancerous sites on the patient's oral mucosa. Areas of the mucosa which are preferentially stained are recognized as characteristic of cancerous or precancerous conditions.

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In a second embodiment of the method for screening epithelial cancer, the liquid testing reagent is introduced into the mouth of a patient and the patient is advised to rinse and gargle. If a suspected site is detected after this first rinse application, the administering clinician applies the testing reagent to the suspected sites by application with the prepackaged swabstick. Preferably, application of the liquid testing reagent by administration with the prepackaged swabstick occurs 10 to 14 days after the initial rinse to reduce the likelihood of false positives.

In a third embodiment of the present method for screening for epithelial cancer, the rinse procedure is replaced by preferentially applying the liquid testing reagent to suspected cancerous or precancerous sites by application with the prepackaged swabstick of the present invention. By providing the administering clinician with a prepackaged swabstick for both the first screening administration and the sequential validating procedure, the messy and inconvenient step of rinsing the patient's mouth with the liquid testing reagent is thereby eliminated.

As will be apparent to those skilled in the art, my invention is not limited to a specific treatment method of specific solutions. Instead, it is generally applicable to any epithelial cancer detection procedure which employs a testing reagent, without limitation on the specific testing reagent employed.

Having described my invention in such terms as to enable those skilled in the art to understand and practice it, and having identified the presently preferred embodiments thereof, I claim:

CLAIMS

1. In a method for screening for epithelial cancer, according to a procedure which includes the step of applying a liquid testing reagent of a preselected concentration to suspected cancerous or precancerous sites, the improvement comprising:

- 5 applying such reagent with a prepackaged swab, including a package encasing an absorbent swab, said swab disposed at an extremity of a handle and being saturated with the liquid testing reagent to permit direct application of the reagent directly from its prepackaged form, in accordance with the screening procedure, without further mixing or
- 10 measuring steps.

2. A prepackaged swabstick for performing routine screening procedures to detect possible epithelial cancer, said procedures including the step of applying to suspected cancerous or precancerous sites a liquid testing reagent, said prepackaged swabstick including a packet encasing an absorbent swab, said
- 5 swab disposed at an extremity of a handle and being saturated with a liquid testing reagent to permit direct dispensation of the reagent directly from its prepackaged form, in accordance with the screening procedure, without further mixing or measuring steps.

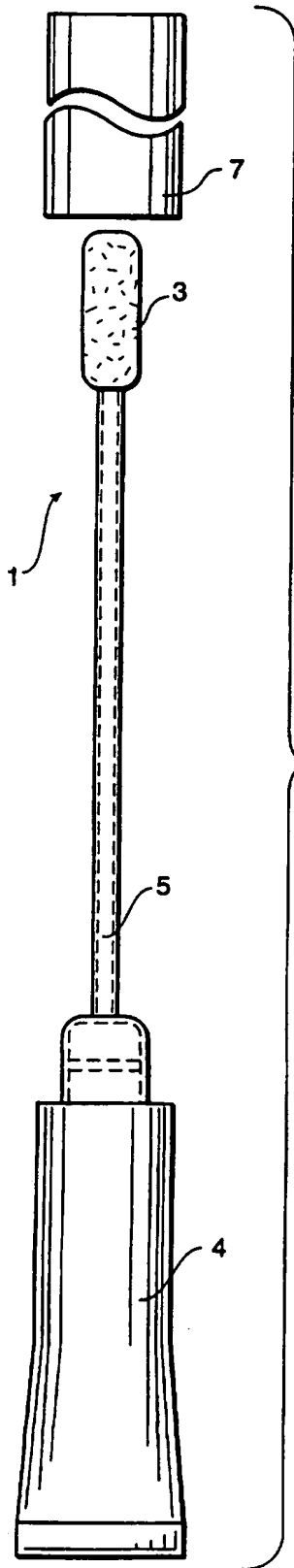


FIG. 1

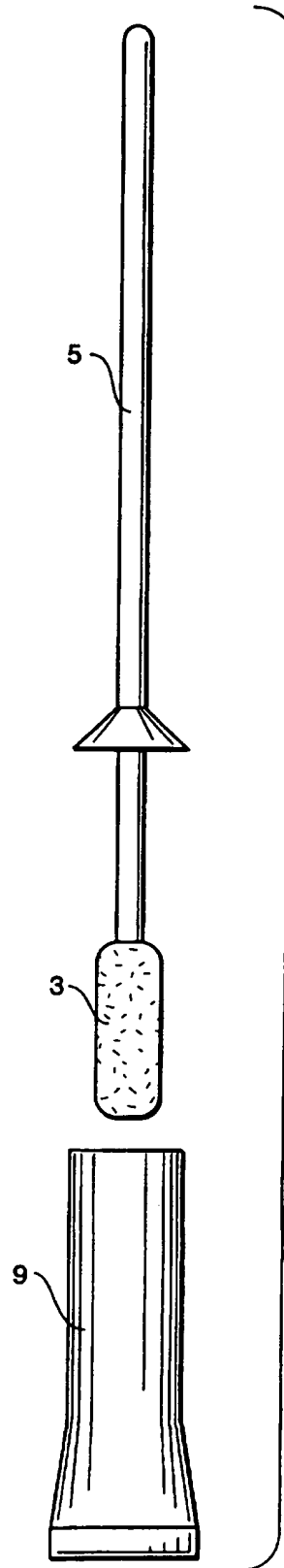


FIG. 2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/02734

A. CLASSIFICATION OF SUBJECT MATTER IPC(6) :A61M 35/00 US CL :604/1 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 424/7.1; 604/1-3 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Extra Sheet.		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 5,372,801 (MALMROS ET AL.) 13 December 1994, see column 7 lines 24-62.	1, 2
Y	US, A, 5,378,226 (HANIFL ET AL.) 03 January 1995, see entire document.	1, 2
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* "A"	Special categories of cited documents: document defining the general state of the art which is not considered to be part of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230		Authorized officer ROBERT CLARKE <i>Tom Hill</i> Telephone No. (703) 308-2908

INTERNATIONAL SEARCH REPORT

International application No.

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B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, BIOSIS, MEDLINE, CAPLUS, EMBASE, CMOPENDEX, EMA, WPIDS

Search Terms: cancer, toluidine, oral, dye or ink, swab, test? or diagnos? muc? human, cheek.